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First Results on Cell Irradiation with laser-driven protons on the TARANIS system

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Abstract. The ultra short duration of laser-driven multi-MeV ion bursts offers the possibility of radiobiological studies at extremely high dose rates. Employing the TARANIS Terawatt laser at Queen's University, the effect of proton irradiation at MeV-range energies on live cells has been investigated at dose rates exceeding 10^9 Gy/s as a single exposure. A clonogenic assay showed consistent lethal effects on V-79 live cells, which, even at these dose rates, appear to be in line with previously published results employing conventional sources. A Relative Biological Effectiveness (RBE) of 1.4 ± 0.2 at 10% survival is estimated from a comparison with a 225 kVp X-ray source.

INTRODUCTION

In view of their properties, laser-driven ion beams have the potential to be employed in a number of innovative applications in the scientific, technological and medical areas. Among these, a particularly high-profile application is particle therapy for cancer treatment, which however requires significant improvements from current performances of laser-driven accelerators. The focus of current research in this field is on developing suitable strategies enabling laser-accelerated ions to match these requirements, while exploiting some of the unique features of a laser-driven process.

The perspective of their future use in cancer therapy demands extensive testing of the biological effects of laser-driven beams, which have very different properties and potentially different radiobiological effectiveness from conventional beams. Employing the TARANIS laser at Queen's University, we have initiated campaigns investigating the effect of proton irradiation at MeV energy range on V-79 cells at dose rates exceeding 10^9 Gy/s in a single exposure [1]. Dispersion of the broadband laser driven multi-MeV proton beam by using static magnetic field, allows simultaneous irradiation of a number of cell spots with different doses on ns timescale. A Relative Biological Effectiveness (RBE) of 1.4 ± 0.2 at 10% survival is estimated from a comparison with a conventional 225 KV X-ray source.

RADIOBIOLOGICAL EFFECTIVENESS OF LASER DRIVEN PULSED HIGH DOSE RATE RADIOTHERAPY

The use of ion beams in cancer radiotherapy exploits the advantageous energy deposition properties of ions as compared to more commonly used X-rays. Unlike X-rays, ions are able to deliver lethal amount of doses into the target tumour while limiting harm to the surrounding healthy tissues. Hadron-therapy has been widely recognized across the globe and several clinical facilities, employing mainly protons from synchrotron, cyclotron or linac accelerators are operational and routinely treating a significant number of patients. The idea of future facilities based on laser driven ion accelerators has been proposed as a way of reducing complexity and cost. Significant effort is ongoing to demonstrate the ion beam parameters required to make this proposition viable. Meanwhile, several groups have started preliminary work on the methodology and viability of using laser driven ion source for cell irradiation experiments.

The ultra-short (ns) duration of laser-driven multi-MeV ion bursts offers the possibility of radiobiological studies at extremely high dose rates, which is virtually unknown and warrants investigation at the cellular level.

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In previous studies of dose-dependent cell damage employing ion bursts accelerated by fs laser systems, e.g. in [2], doses in the Gy range have been delivered to the cells in several fractions. Although each pulse delivered a fraction of a Gy in a short time (tens of ns), the average dose rate over a Gy-level exposure was in the Gy/s range, i.e. not dissimilar from the dose rate normally used in radiobiology with conventional proton sources. Employing the TARANIS laser of Queen's University Belfast, a quantitative study was carried out in order to study dose-dependent biological effects of MeV protons on cells (V79 Chinese Hamster cell line) in the ultrahigh dose-rate regime ($> 10^9$ Gy/s), with the dose (up to 5 Gy) delivered in a single exposure.

The setup of the experiment is shown in the Fig. 1(a). The laser was focused by an $f/3$ off-axis parabola on 10 μm Al foils, leading to an intensity on target of the order of 10^{19} W/cm². At this intensity regime, the protons are accelerated by the TNSA mechanism, which leads to broadband proton energy spectra, typically with particle numbers exponentially decreasing up to the cut-off energy. In our case, up to 10^{11} /MeV/Sr protons were produced at 3 MeV energy, which allowed delivering high doses (several Gys) to cell samples to be attained in a single shot. Proton energy selection on cells was done by employing strong magnetic field with an input aperture close to the target. The cells were placed outside the vacuum chamber, followed by highly sensitive EBT type radiochromic film for in-situ dosimetry [3]. In this setup, four cell dots were placed in a row in order to expose simultaneously by different energy protons (ranging from 2.5 MeV to 5 MeV) at different dose values (a fraction of Gy to several Gy). Two control cell dots placed in the same cell holder at a position well shielded from proton exposure. After the irradiation, each cell dots were processed in a similar fashion for clonogenic assay.

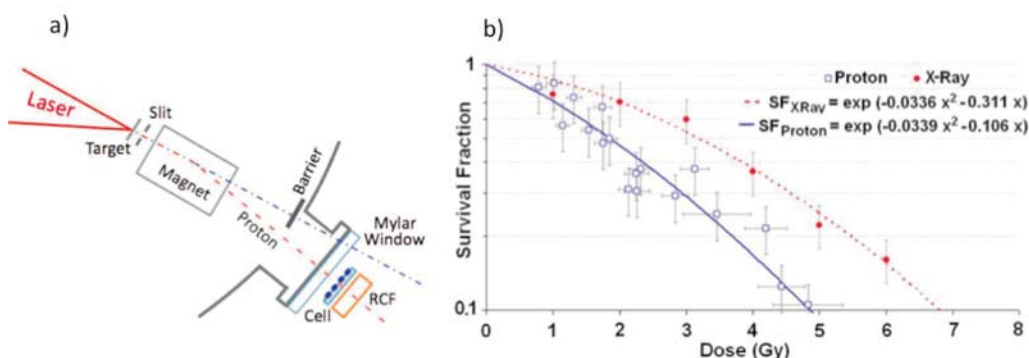


FIGURE 1. a) Schematic of the experimental setup. **b)** Survival curve for the V79 cells obtained using protons with energies in the range 1 – 5 MeV. A curve obtained by X-ray irradiation on the same cells, and using the same cell processing methodology, is also shown for comparison.

The Surviving Fractions (SF) were calculated as $SF = \text{Number of Colonies} / (\text{Number of Cultured cell} \times PE)$, where PE is the plating efficiency. Finally, for comparison, cell samples prepared according to the same procedure were irradiated with a calibrated X-ray source (XRAD 225 kVp from PXI Inc.) shielded by a 2 mm thick Cu filter in order to cut the low energy part of the spectrum. The resulting survival curve is shown in Fig. 1(b), where the data has been fitted using a linear-quadratic model. The uncertainty in dose is mainly due to the finite size (2.5 mm) of the cell dots, while the error bars of the SF refer to the uncertainty associated with the method used in processing the cells and it is about 20% of the data point value.

As expected, the survival curves shown in the Fig. 1(b) indicate higher biological efficiency of protons with respect to X-rays. From the comparison between proton and X-ray data, a Relative Biological Effectiveness (RBE) of 1.4 ± 0.2 can be calculated at 10% SF. Direct comparison with results available in the literature is not straightforward, as the points in the curve are obtained using different cell dots irradiated at central energies in the range 1 - 5 MeV. However, the measured RBE value is similar to that published for mono-energetic proton inactivation of V79 cells in MeV energy range [4].

The data indicates that, at the dose levels investigated, the ultrahigh dose rate employed has no significant effect on cell survival. This is an encouraging result in view of potential future therapeutic use of ultra short bursts of laser-driven ions, as, in realistic arrangements, proton pulse durations on the cells will be of ns order or more, as employed in the measurements reported here. We note that similar conclusions on independence of survival results from dose rate (although employing a different cell line and protons with different LET) have been very recently reached in experiments employing a pulsed ion microbeam [5] and laser-produced beams focused with quadrupole magnets [6], operating at similar dose rates and pulse durations as in the experiment presented here. We believe that, with an optimized set-up, it will be possible in the near future to increase the

dose rate deliverable by laser-accelerated protons by a further 2 orders of magnitude, which will allow testing for the emergence of collective effects as predicted in [7].

CONCLUSIONS

Ion acceleration driven by high power laser has been a highly active area of research for over a decade and has been encouraged by the rapid development in laser technology and related areas. The currently observed ion beams show appealing properties in terms of ion energy, divergence and fast energy scaling, and offer high promise for further progress in the near future. This prospective highlights studies of biological effectiveness of laser driven, short-burst ion beams as timely and relevant. Preliminary work of our group in this direction is presented studying RBE of laser driven protons irradiating V-79 cells at ultra-high dose rate.

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